Remarks/Arguments

The foregoing amendments to the claims are of a formal nature, and do not add new matter. Claims 119-138 are pending in this application and are rejected on various grounds. Claims 127-128, 132-134 have been canceled without prejudice or disclaimer to claim their subject matter in subsequent continuation or divisional applications. Claims 139-145 have been added, support for which is found in canceled Claim 132 and in the instant specification at page 285, line 11 onwards. Entry of these claims is respectfully requested. Accordingly, Claims 119-126, 129-131, 135-142 are now pending in this application. Claims 119-128 have been amended for clarity with the recitation "wherein said nucleic acid is amplified in lung or colon tumors" support for which is found in Example 170 of the instant specification, especially in Table 8 and 9B. The rejections to the presently pending claims are respectfully traversed.

Priority

Applicants rely on the 'Gene amplification' assay for patentable utility of this case, first disclosed in International Application PCT/US/00/03565, filed February 11, 2000, priority for which has been claimed in this application. Applicants further submit that the subject matter defined in that application provides a specific and substantial asserted utility or a well established utility for the claimed invention for the same reasons as those discussed below under the utility section for the present application. Hence, the present application is at least entitled to an effective filing date of **February 11, 2000.**

Information Disclosure Statement

The Examiner had objected to the previously submitted IDS because it did not comply with the requirements of 37 C.F.R. § 1.98(a)(2). Applicants hereby submit a new IDS separately enlisting each accession number for the sequence, the reference and the database where the sequence is available, from the previously filed Blast report of 5/31/2002 which complies with 37 C.F.R. § 1.98(a)(2). Consideration of this Information Disclosure Statement is respectfully requested.

Specification

The disclosure has been amended to delete all "embedded hyperlink and/or other form of browser-executable code." Accordingly, Applicants believe that all objections to the specification have been overcome.

Claim Rejections – 35 USC § 101 and § 112, first paragraph

A. Claims 119-128 and 132-138 were rejected under 35 U.S.C. §101 allegedly "because the claimed invention is not supported by a specific, substantial and credible asserted utility or well established utility."

B. Claims 119-124 and 132-138 were rejected under 35 U.S.C. §112, first paragraph allegedly "since the claimed invention is not supported by either a substantially asserted utility or a well established utility, one skilled in the art clearly would not know how to use the claimed invention."

Regarding the gene amplification data, the Examiner acknowledges that SEQ ID NO: 407 can be used for diagnostic purposes but asserts that any other nucleic acid or variants, even degenerate variants encoding the same protein have not been shown to be higher in tumor samples compared to normal samples. The Examiner further quotes Pennica *et al.*, to show that "it does not necessarily follow that an increase in gene copy number results in increased gene expression and increase protein expression." For the reasons outlined below, Applicants respectfully traverse these rejections.

Utility Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility."

Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly

is the benefit derived by the public from an invention with substantial utility." In explaining the "substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance with the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: **"If the (A)pplicant has asserted that the claimed invention is useful for any particular practical purpose . . . and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."**

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record . . . that is probative of the Applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

To overcome the presumption of truth based on an assertion of utility by the Applicant, the Examiner must establish that **it is more likely than not** that one of ordinary skill in the art would doubt the truth of the statement of utility. **Absolute predictability is not a requirement.**

Only after the Examiner has made a proper *prima facie* showing of lack of utility, does the burden of rebuttal shift to the applicant. The issue will then be decided on the totality of evidence.

Arguments

Initially, Applicants submit that the cancellation of Claims 127-128 and 132-134, without prejudice or disclaimer, renders this rejection moot to these claims. Further, without acquiescing

to the propriety of this rejection, Applicants have amended Claims 119-123 to recite a functional recitation: "wherein said nucleic acid is amplified in lung or colon tumors".

asserts that any other nucleic acid or variants, even degenerate variants encoding the same protein have not been shown to be higher in tumor samples compared to normal samples. The Examiner further quotes Pennica *et al.*, to show that "it does not necessarily follow that an increase in gene copy number results in increased gene expression and increase protein expression."

In response to the Examiner's rejections, Applicants entirely disagree with the Examiner's conclusion that "it does not necessarily follow that an increase in gene copy number results in increased **gene expression** and increase **protein** expression" (emphasis added) but, for the sake of brevity, since "gene expression or polypeptide expression" have no bearing on the instant claims that claim nucleic acids, they do not discuss this point further. Instead, Applicants respectfully point out that the instantly amended claims are directed to naturally occurring **nucleic acids** encoding PRO1245 that are amplified in lung or colon cancer, and not to polypeptides or mRNA - products of gene expression. Hence, in this instance, this rejection which addresses gene/ polypeptide expression based on the teachings of Pennica *et al.* which discuss gene expression, is misplaced. Instead, Applicants submit that, based on the instant disclosure, which details how to make and use nucleic acid variants (see pages 308-311), and the advanced knowledge in the art at the time of filing, one skilled in the art would know exactly what nucleic acid variants the instant claims encompass and would know how to make and use these nucleic acids for the diagnosis of lung or colon cancer without undue experimentation; for example, by using diagnostic methods based on hybridization to such amplified sequences.

Applicants have clearly demonstrated utility for the PRO1245 nucleic acid as a lung or colon tumor markers. Accordingly, the present 35 U.S.C. §101and §112, first paragraph, utility rejections should be withdrawn.

Claim Rejections - 35 USC § 112, first paragraph- written description

Claims 119-124 and 132-138 are rejected under 35 U.S.C. 112, first paragraph because allegedly, the subject matter was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time of filing.

The Legal Standard for Written Description

The well- established test for sufficiency of support under the written description requirement of 35 U.S.C. §112, first paragraph, is whether the disclosure "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *In re* Kaslow, 707 F.2d 1366, 1375, 212 USPQ 1089, 1096 (Fed. Cir. 1983); see also Vas-Cath, Inc. v. Mahurkar, 935 F. 2d at 1563, 19 USPQ2d at 1116 (Fed. cir. 1991). The adequacy of written description support is a factual issue and is to be determined on a case-by-case basis. see *e.g.*, Vas-Cath, Inc. v. Mahurkar, 935 F. 2d at 1563, 19 USPQ2d at 1116 (Fed. cir. 1991). The factual determination in a written description analysis depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure. Union Oil v. Atlantic Richfield Co., 208 F. 3d 989, 996 (Fed. Cir. 2000).

Arguments

As noted above, whether the Applicants were in possession of the invention as of the effective filing date of an application is a factual determination, reached by the consideration of a number of factors, including the level of knowledge and skill in the art, and the teaching provided by the specification. The inventor is not required to describe every single detail of his/her invention. An Applicant's disclosure obligation varies according to the art to which the invention pertains.

The present invention pertains to the field of recombinant DNA/protein technology. It is well established that the level of skill in this field is very high since a representative person of skill is generally a Ph.D. scientist with several years of experience. Accordingly, the teaching imparted in the specification must be evaluated through the eyes of a highly skilled artisan as of the date the invention was made. The instant invention, defined by the claims, concerns polypeptides having 80%, 85%, 90%, 95% or 99% sequence identity with the disclosed polypeptide sequence SEQ ID NO: 408 and further, with the functional recitation: "wherein the nucleic acid encoding said polypeptide is amplified in lung or colon tumors." Specific utility has been asserted in the present invention based on the amplification the nucleic acids encoding PRO1245 and the pending claims recite this functional feature. Thus, the pending claims are drawn to a genus of polypeptides defined both by sequence and functional identity. It would have been obvious to one skilled in the art at the effective priority date, in view of Applicant's possession of the PRO1245 sequence (SEQ ID NO: 408), that the Applicant possessed obvious

variations and adaptations of SEQ ID NO: 408 as well, at the time of filing. Based on the detailed description of the cloning and expression of variants of PRO1245 in the specification, the description of the gene amplification assay and description of testing the ability of test variant polypeptides in the assay, the actual reduction to practice of sequence SEQ ID NO: 408 and the knowledge in the art, Applicants submit that one of skilled in the art would know that Applicants possessed the invention as claimed in the instant claims.

Hence, Applicants request that the present rejection to the present claims be reconsidered and withdrawn.

Claim Rejections-35 USC § 112, second paragraph

Claims 132-134 was rejected as vague and indefinite for reciting the term "hybridizes" and "stringent" without recitation of any conditions in each case.

Applicants have canceled claims 132-134 and hence these rejections are moot. Applicants have added claims 139-145 that recite the exact "stringent conditions" under which hybridization was performed. Support for this amendment is found in the specification at least at page 312, line 33 to page 313, line 5 and in canceled claim 132. Accordingly, Applicants submit that the claims are definite and respectfully request that this rejection be withdrawn.

Claim Rejections - 35 USC § 102

a. Claims 119-131 are rejected under 35 U.S.C. §102(b) as being anticipated by as being anticipated by WO 99/63088, dated December/1999; WO 99/60160, dated November/1999; WO 00/00610, dated June/2000.

Based on the discussions above, Applicants believe that they are entitled to at least an effective date of **February 11, 2000** for this application. Accordingly, WO 99/63088, dated December/1999 and WO 99/60160, dated November/1999 are **102(a)** art instead. Applicants submit that WO 99/63088, dated December/1999 is the Applicants own art and can be overcome with an affidavit if necessary. Further, Applicants submit that the nucleic acids and polypeptides of SEQ ID NO: 407 and 408 were cloned, sequenced and disclosed in U.S. provisional application 60/097978, filed 8/26/1998 as SEQ ID NOs: 2 and 1 (Figures 2 and 1) and priority has been claimed to this provisional application in this application as well. Hence, the Applicants invention of PRO1245 and its encoding nucleic acids predate the WO 99/60160, dated

November/1999 reference as well. If necessary, a Declaration can be submitted to reiterate this point.

Accordingly, Applicants submit that the above cited art are not prior art and this rejection should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-2730P1C70). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: August 13, 2004

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